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EXAMINER

SINES, BRIAN J

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1743

15

DATE MAILED: 11/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/466,325

Applicant(s)

BRISCOE ET AL.

Examiner

Brian J. Sines

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 8/13/2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,6-8,10-12,14-23 and 26-35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,6-8,10-12,14-23 and 26-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2, 6 – 8, 10, 14, 17 – 23 and 28 – 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. (US 5,849,208) in view of Wilding et al. (US 5,587,128 A). Regarding claim 1, Hayes et al. teach an apparatus 10 comprising: a supporting substrate 20; a plurality of separate well structures 40-42 comprising a thermal conducting layer and wherein the well structures are separated by a thermal insulating layer contained in regions defined by 30a - 30c; a means for heating 50-52 each well structure in thermal contact with the thermal conducting layer comprising each well; a means for cooling 90 each well structure in thermal contact with the thermal conducting layer comprising each well; a means for monitoring the temperature 182 of the contents of each well structure in thermal contact with the

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thermal conducting layer comprising each well (col. 1, line 1 – col. 16, line 7). Hayes et al. teach a spacer section 58, which is a thermal conducting layer, that electrically insulates the heating element 54 from the contents of the reaction chamber 40, but is thin enough to permit rapid and efficient heat transfer from the heating element 54 to any material contained in the reaction chamber (col. 5, line 62 – col. 6, line 3). Hayes et al. do not specifically teach that the device may be manufactured from a ceramic material. Hayes et al. do teach that the apparatus may be manufactured from a polymeric plastic material, such as polyimide (col. 4, lines 8 – 25). Wilding et al. teach microfluidic chip device that may be comprised of either glass, silicon, plastic or ceramic materials (col. 1, lines 48 – 59; col. 7, lines 22 – 38). Wilding et al. teach that the device may be utilized in polynucleotide amplification reactions, such as the polymerase chain reaction (PCR) (col. 1, lines 19 – 26). Furthermore, ceramics are known corrosion resistant and heat-resistant, or thermally nonconductive, insulative materials. Therefore, it would have been obvious to manufacture the supporting substrate from a ceramic material and to incorporate this ceramic material as a thermally insulating layer between each of the wells, since the Courts have held that the selection of a known material based upon the suitability of the material for the intended use is within the ambit of one of ordinary skill in the art. See *In re Leshin*, 125 USPQ 416 (CCPA 1960). The motivation to use a ceramic material in the fabrication of the apparatus taught by Hayes et al. would have been to facilitate effective thermal isolation of each of the wells, since each of the wells may be independently controlled using different temperature cycles. Regarding claim 2, Hayes et al. teach that the

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apparatus may be especially useful for performing and analyzing the results of a polymerase chain reaction (PCR) (see Abstract). Regarding claim 6, Hayes et al. teach a spacer section 58, which is a thermal conducting layer, that electrically insulates the resistive heating element 54 from the contents of the reaction chamber 40, but is thin enough to permit rapid and efficient heat transfer from the heating element 54 to any material contained in the reaction chamber or well structures (col. 5, line 28 – col. 6, line 3). The thermal conducting layer 58 contains, or holds within a limit, the resistive heating element 54. The motivation to incorporate a thermal conducting layer containing an integrated resistive heater would have been to provide for effective temperature control for each of the well structures. Therefore, it would have been obvious to incorporate a thermal conducting layer, which contains, or has within an integrated resistive heater, with the well structures in the apparatus. Regarding claim 7, Hayes et al. teach that the well structures, or reaction chambers 40-42, are partially formed from a spacer section 58, which is a thermal conducting layer, that electrically insulates the resistive heating element 54 from the contents of the reaction chamber 40, but is thin enough to permit rapid and efficient heat transfer from the heating element 54 to any material contained in the reaction chamber or well structures (col. 5, line 28 – col. 6, line 3). Regarding claim 8, Hayes et al. teach that the supporting substrate 20 may comprise polyimide (col. 7, lines 46 - 50). Hayes et al recognizes the benefits and suitability, e.g., temperature stability, of utilizing a polymer material, such as polyimide, in the fabrication of the supporting substrate of an apparatus used in chemical analysis, such as PCR. Furthermore, ceramics are known corrosion resistant and heat-resistant,

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or thermally nonconductive, insulative materials. The motivation to use a ceramic material in the fabrication of a thermal insulating layer would have been to effectively thermally isolate each well structure in order to facilitate efficient independent temperature cycling control for each well. Therefore, it would have been obvious to incorporate a thermal insulating material made from a polymeric plastic material, and including other materials such as glass or ceramic, since the Courts have held that the selection of a known material based upon its suitability for the intended use is within the ambit of one of ordinary skill in the art. See *In re Leshin*, 125 USPQ 416 (CCPA 1960). Regarding claim 10, copper is a known material which is capable of electrically insulating the resistive heating element 54. Hayes et al. teach that the resistive heating element may be formed from any of a variety of electrically resistive and therefore thermally conductive materials, such as nickel/chromium alloys, suitably doped semiconductors, etc. (col. 5, lines 51 – 61). The motivation to use either copper, or a nickel alloy, as a thermal conducting material in the fabrication of the well structures would have been to facilitate effective heat transfer and temperature control for the apparatus. Therefore, it would have been obvious to utilize either undoped silicon, modified plastics, silver, silver palladium, copper, nickel-molybdenum, platinum, or gold as the thermal conducting material since the Courts have held that the selection of a known material based upon its suitability for the intended use is within the ambit of one of ordinary skill in the art. See *In re Leshin*, 125 USPQ 416 (CCPA 1960). Regarding claim 14, Hayes et al. teach that controllable resistance heater 50, which is shown in greater detail in figure 2 and illustrative of heaters 50-52, is integrally formed within the

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substrate. Hayes et al. teach that any heater having a heating element in thermal contact with a reaction chamber is suitable (col. 5, lines 29 – 36). Temperature control within these microfluidic devices are generally supplied by thin film resistive heaters. The motivation to incorporate a thin film resistive heater within the integrated heating system would have been to facilitate the effective temperature control for the reaction wells using a proven and suitable heating means well known in the art. Therefore, it would have been obvious to incorporate an integrated heating system, which incorporates a thin film resistive heater. Regarding claims 17 and 18, Hayes et al. teach that the apparatus is controlled using a programmable controller (col. 14, line 5 – col. 16, line 7). One of ordinary skill in the art would have contemplated a row and column addressing or an individual electrical addressing system in order to keep record of the status of each of the reaction wells of the structure during analysis. The motivation to use either a column and row addressing system or an individual addressing system would have been to effectively monitor and control each of the reaction wells during the temperature cycling process. Therefore, it would have been obvious to incorporate an integrated heating system, which utilizes either column and row addressing or individual electrical addressing. Regarding claims 19 – 22, Hayes et al. teach a heat sink 90 is secured to the second major face 24 with a thermally conductive adhesive 92. The heat sink may either be a conventional thermo-electric device, which is an active cooling system, or have a finned surface, which is a passive cooling system, or both. Hayes et al teach the use of thermo-electric coolers (col. 4, line 63 – col. 5, line 4). The motivation to incorporate an integrated cooling system within the apparatus

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would have been to facilitate effective temperature cycling control for the reaction wells using a proven and suitable cooling means well known in the art. Therefore, it would have been obvious to incorporate an integrated passive or active cooling system for each well. Furthermore, it would have been obvious for one of ordinary skill in the art to incorporate an integrated cooling system, which comprises either a metal plate, an array of metal discs, or a thermo-electric cooler in thermal contact with each of the well structures of the apparatus. Hayes et al. teach a microfluidic dispensing means for delivering reagents into each well structure (col. 11, lines 42 – 64). Regarding claim 28, Hayes et al. teach that the well structures may be sealed or covered (col. 12, lines 47 – 62). The motivation to incorporate sealed well structures with the apparatus would have been to prevent any of the reagents from evaporating. Therefore, it would have been obvious to incorporate sealed well structures using a cover into the apparatus.

Regarding claims 29 and 30, Hayes et al. teach that heater 154 may assume any geometry which places it in thermal contact with the reaction chamber (col. 9, lines 5-23). Hayes et al. also teach that a thermo-electric heater can be incorporated directly into the substrate (col. 10, lines 13 – 19). The motivation to incorporate a cover which further comprises a heating means for heating the well structures would have been to facilitate effective temperature control for the device. Therefore, it would have been obvious to incorporate a cover further comprising an integrated heating means for effectively heating the well structures of the apparatus. Regarding claims 31, 32 and 33, Hayes et al. teach the use of wire thermocouples and thin film thermocouples for temperature sensing. Thin film thermocouples may comprise a separate layer within

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the substrate 120. Thin film thermocouples may also be incorporated into portions of a polyimide layer (col. 5, lines 59 – 61; col. 8, lines 60 – 65). The motivation to incorporate a means for monitoring the contents of each of the well structures would have been to facilitate effective temperature sensing. Therefore, it would have been obvious to incorporate a means for monitoring the temperature of the contents of each well structure which is a resistive thermal detector, or a thermocouple, which can be molded into the plastic of the apparatus. Hayes et al. teach the incorporation of conductive pathways or interconnect pads 156 a, 156b which extend to side 122b for connection to an external power source.

Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. in view of Wilding et al. as applied to claims 1, 2, 6 – 8, 10, 14, 17 – 23 and 28 – 33 above, and further in view of Anderson et al. (US 6,168,948 B1). Hayes et al. and Wilding et al. do not teach the use of parylene as a coating compound. Anderson et al. do teach the coating of surfaces with parylene (col. 20, lines 27 – 44). The motivation to use parylene as a coating compound would have been to provide a non-stick coating for the system to prevent the adhesion of the components of the molecular reaction with the system components. Therefore, it would have been obvious to use parylene as a coating for the thermal insulating, or conducting materials, comprising the well structures of the apparatus.

Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. and Wilding et al. as applied to claims 1, 2, 6 – 8, 10, 14, 17 – 23 and 28 – 33 above, and further in view of Burns et al. (US 6,057,149). Hayes et al. and

Wilding et al. do not specifically teach the use of a metal wire resistive heater, which is integrated into the thermal insulating material comprising the supporting substrate of the device. Metal wire resistive heating elements are generally well known in the art. The motivation to incorporate a metal wire resistive heater within the integrated heating system would have been to facilitate the effective temperature control for the reaction wells using a proven and suitable heating means well known in the art. Therefore, it would have been obvious to incorporate a metal wire resistive heater within the integrated heating system. Furthermore, regarding claim 16, Hayes teach that the heating elements are formed integrally with the substrate (col. 13, lines 1 –4). The motivation to integrate the metal wire resistive heater into the thermal insulating material comprising the supporting substrate would have been to facilitate the effective temperature control for the reaction wells using a proven and suitable heating means well known in the art. Therefore, it would have been obvious to integrate a metal wire resistive heater into the thermal insulating material comprising the supporting substrate.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. in view of Wilding et al. as applied to claims 1, 2, 6 – 8, 10, 14, 17 – 23 and 28 – 33 above, and further in view of Kellogg et al. (US 6,063,589). Hayes et al. do teach the use of a thermocouple wire and a thin film thermocouple wire for temperature sensing (col. 8, lines 40 – 65). Hayes et al. and Wilding et al. do not teach the use of an integrated optical or electrochemical sensor system for temperature sensing. Kellogg et al. do teach the use resistive heaters as thermosensors, which utilize screen-printed positive temperature coefficient (PTC) inks, for temperature sensing within a

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microfluidic apparatus (col. 56, lines 34 – 63). The motivation to incorporate an electrochemical temperature sensing system would have been to facilitate the effective temperature measurement and control for the reaction wells using a proven and suitable sensing means well known in the art. Therefore, it would have been obvious to incorporate a means for monitoring the temperature of the molecular interactions in each well structure which is either an electrochemical or an integrated optical system.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. in view of Wilding et al. as applied to claims 1, 2, 6 – 8, 10, 14, 17 – 23 and 28 – 33 above, and further in view of Anderson et al. (US 6,168,948 B1). Hayes et al. and Wilding et al. do not teach that the well structures are sealed using a layer of mineral oil. Anderson et al. do teach the use of mineral oil deposited over the reaction chambers of a microfluidic device as a sealing means. The motivation to use mineral oil as a sealing means for the well structures would have been to prevent excessive evaporation of the sample while allowing the evolution of gas evolution during analysis. Therefore, it would have been obvious to incorporate a mineral oil layer as a means of sealing the well structures of the apparatus.

Response to Arguments

Applicant's arguments filed 8/13/2002 have been fully considered but they are not persuasive.

The recitation in part (a) of claim 1 that the apparatus is fabricated using multi-layer ceramic technology using green-sheet layers is considered a process limitation, and is accorded no patentable weight in the claims to an apparatus. As the structure of

the apparatus, as taught by Hayes et al. in view of Wilding et al., is identical to that of the claims, i.e., comprising a substantially monolithic ceramic structure, it would appear that the method of making the apparatus would also be the same. Process limitations do not add patentability to a structure, which is not distinguished from the prior art. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. See *In re Thorpe*, 777 F.2d 695, 697, 227 USPQ 964, 966 (Fed. Cir. 1985). Furthermore, it should be noted that claim 1 is using open-ended language, i.e. "comprising," which does not exclude additional, or unrecited structural limitations, such as metallic layers for example, as taught by Hayes et al. See *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997). "Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim. See *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); *In re Baxter* 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by

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combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Hayes et al. in view of Wilding et al. teach the materials, such as ceramics, glass and polymeric plastic materials, generally available to one of ordinary skill in the art used in the fabrication of devices used in chemical analysis. The claims recite the incorporation of well known materials, such as ceramic materials (e.g., silicon nitride or glass), in the structure of the device. Both of the devices as taught by Hayes et al. and Wilding et al. are used in performing polymerase chain reactions, which involve temperature cycling. Hayes et al. do teach the use of silicon nitride in the fabrication of such devices (see col. 7, lines 22 – 38; col. 14, lines 15 – 34). One of ordinary skill in the art would have recognized the benefits of using ceramic materials in the fabrication of such a device, since the Courts have held that the selection of a known material based upon the suitability of the material for the intended use is within the ambit of one of ordinary skill in the art. See *In re Leshin*, 125 USPQ 416 (CCPA 1960).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Sines whose telephone number is (703) 305-0401. The examiner can normally be reached on Monday - Friday (11:30 AM - 8 PM EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9310 for regular communications and (703) 872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

BJS
November 3, 2002


Jill Warden
Supervisory Patent Examiner
Technology Center 1700